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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/328,975	06/09/1999	JOHN A. WOLFF	MIRUS009	7574
25032	7590	06/29/2005		
MIRUS CORPORATION 505 SOUTH ROSA RD MADISON, WI 53719			EXAMINER SCHNIZER, RICHARD A	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/328,975

Applicant(s)

WOLFF ET AL.

Examiner

Richard Schnizer, Ph. D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3 and 5-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 5-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 June 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

An amendment was received and entered on 4/18/05. Claims 4 was canceled as requested.

The Declaration of Dr. Trubetskoy was received and entered on 4/18/05. The declaration has been fully considered.

Claims 1, 3, and 5-8 remain pending and are under consideration in this Office Action.

This Action contains new Double Patenting rejections not necessitated by amendment, and so is NON-FINAL.

The previous indication that claim 8 was allowable is withdrawn in view of Double Patenting rejections set forth below.

### ***Rejections Withdrawn***

The rejection of claims 1, and 5-7 under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendment. Note that claim 7 is now indefinite due to the cancellation of claim 4, from which it depends.

The rejection of claims 1, 3, and 5-7 under 35 USC 103 over Curiel in view of Lee is withdrawn in view of Applicant's amendment requiring a "polyanion" in step b) rather than a "charged polymer". The rejection is no longer applicable because the specification requires at page 12, lines 23-27 that a polyanion by definition must have a net negative charge. In contrast, the charged polymer of Curiel consisted of a polylysine polymer conjugated to an anionic peptide. This composition is a graft

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copolymer with a net positive charge, and so cannot be a polyanion as defined by the specification.

### ***Specification***

The declaration of Dr. Trubetskoy under 35 USC 1.132 is sufficient to support the amendments to the specification at page 22, lines 26 and 27, wherein the abbreviation "PAA" is changed to --pAsp--, and on pages 26 and 27 wherein "dextran sulfate" or "DS" was changed to polyacrylic acid. Note that the results in experiments 1-4 on pages 121-122 of the notebook match the data presented in Table I on page 27 of the specification, when averaged.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5- 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 7 are indefinite because they depend from cancelled claim 4.

Claim 6 is indefinite because it recites "the charged polymer" without antecedent basis. Substitution of --polyanion-- for "charged polymer" is suggested.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, and 5-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,881,576. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of '576 is:

1. A process for enhancing delivery of a polyion to a cell, comprising: forming a polyampholyte having a net charge, in the presence of a polyion; and, delivering the complex into a cell.

The specification, in support of this claim, discloses at column 6, lines 44-56 Example 1 which is directed to a general procedure for the formation of a polyampholyte in the presence of DNA:

General procedure for the formation of the polyampholyte in the presence of DNA. (Crosslinking of polycation and polyanion layers on the DNA/PLL/SPLL particles using 1[3-(dimethylamino)propyl]-3-ethyl carbodiimide (EDC) and sulfo-N-hydroxysuccinimide (SNHS). Plasmid DNA (pCILuc) and PLL (M.w. 46 kDa) were mixed in a charge ratio 1:3 (100 ug and 190 ug respectively in 0.5 ml of 20 mM MES, pH 6.5. Succinylated PLL (SPLL) was activated with EDC/SNHS in 50 ul of unbuffered solution at pH 5.0 for 10 min (690 ug SPLL, 1.4 mg EDC, 700 ug SNHS). Then the DNA/PLL complex and activated SPLL were mixed (DNA:PLL:SPLL charge ratio 1:3:10) and the mixture was incubated overnight at room temperature.

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Accordingly claim 1 of '576 embraces a method of forming a complex between a nucleic acid and a polycation wherein the complex has a net charge less negative than the nucleic acid, and subsequently associating with that complex a polyanion in sufficient amount to give the complex a net negative charge. The instant claims do not exclude the step of forming a polyampholyte by crosslinking the polyanion to the polycation, so '576 claim 1 and dependents render it obvious, particularly in view of '576 claim 6 which requires delivery of the complex in vivo. The limitations of instant claim 3 (polycation = polylysine or polyethylenimine) are found in '576 claim 2, as is the limitation of instant claim 6, requiring block copolymers. The limitations of instant claim 5 are found in '576 claim 4. Claim 8 is included in this rejection because the ternary complex of '576 Example 1 appears to comprise a polyanion of at least 80 monomeric units. The polyanion is disclosed at column 6, line 51 as succinylated PLL, and PLL is defined at column 6, line 49 as having a molecular weight of 46 kDa. Assuming a monomer molecular weight of 128 g/mol per lysine monomer, the PLL used is about 360 monomers in length.

Claims 1, 3, and 6-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 and 11-15 of U.S. Patent No. 6,740,643 in view of Lee et al (WO 97/00965, published 1/9/97). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of '643 is drawn to:

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A process for obtaining an expression product by delivering a polynucleotide to a cell, comprising: a) associating a noncovalent amphiphilic polyelectrolyte, a cyclodextrin, and a polynucleotide thereby forming a complex, wherein the noncovalent amphiphilic polyelectrolyte consists of a polymeric amphiphile binding agent and charged amphiphiles; and b) delivering the complex to the cell; and, c) expressing the polynucleotide.

It is clear in view of the specification at the paragraph bridging columns 16 and 17 that claim 1 embraces a method of forming a complex between polylysine and a nucleic acid in the presence of a cyclodextrin, and subsequently recharging the complex by addition of a cyclodextrin-epichlorohydrin copolymer that is rendered polyanionic by addition of 4-t-butylbenzoic acid.

'643 does not explicitly teach that recharged complexes must have a net negative charge.

Lee taught that targeted cationic nucleic acid delivery complexes allow non-specific, non-targeted cellular uptake due to the fact that cells generally have a negative surface charge. Despite the presence of a targeting ligand, the charge attraction between positively charged complexes and negatively charged cells leads to non-specific interactions and uptake. Lee taught that this problem could be avoided by rendering targeted delivery complexes negative in net charge. See page 2, lines 11-16, and page 9, lines 18-25.

In view of the '643 specification at column 23, line 51 to column 4, line 50, the claimed compositions may comprise targeting signals. As a result it would have been obvious to one of ordinary skill in the art at the time of the invention to recharge a targeted polycation/nucleic acid complex by addition of an anionic cyclodextrin-epichlorohydrin copolymer, and to adjust the amount of anionic copolymer added such that the final charge of the recharged complex was negative. One would have been

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motivated to do so in order to increase the efficiency of targeting as taught by Lee above.

Claim 8 is included in this rejection because the '643 specification defines "polymer" at column 26, lines 57-60 as having more than 80 monomers. The term "copolymer" is used to describe the polyanion disclosed at the paragraph bridging columns 16 and 17, so it is considered to have more than 80 monomers.

Claims 1, 3, and 5-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,740,336. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claim 1 of '336 is drawn to:

A process for generating multilayer particles for delivering a polynucleotide to cell, comprising: condensing a polymer with an oppositely charged polymer to form a particle; and, sequentially adding oppositely charged polymers at the particle forming at least three layers of polymers wherein at least one of the polymers is the polynucleotide.

The specification discloses that the first recited polymer may be a nucleic acid, the second a polycation, and the third, used to recharge the polycation/nucleic acid complex, may be any of the polyanions in instant claims 5-7. See e.g. column 5, lines 1-14:

A wide a variety of polyanions can be used to recharge the DNA/polycation particles comprising: succinylated PLL, succinylated PEI (branched), polyglutamic acid, polyaspartic acid, polyacrylic acid, polymethacrylic acid, polyethylacrylic acid, polypropylacrylic acid, polybutylacrylic acid, polymaleic acid, dextran sulfate, heparin, hyaluronic acid, polysulfates, polysulfonates, polyvinyl phosphoric acid, polyvinyl phosphonic acid, copolymers of polymaleic acid, polyhydroxybutyric acid, acidic polycarbohydrates, DNA, RNA, negatively charged proteins, pegylated derivatives of above polyanions, pegylated derivatives carrying specific ligands, block and graft copolymers of polyanions, any hydrophilic polymers (PEG, poly(vinylpyrrolidone), poly(acrylamide), etc), and other water-soluble polyanions.

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The specification teaches that the polycation may be polylysine or polyethylenimine.

See column 6, lines 6-12 and paragraph bridging columns 11 and 12. Claim 6 requires that the particle formed must be negatively charged. As a result the methods of instant claims 1, 3, and 5-7 are not patentably distinct from those of claims 1-3 of '336.

Claims 1, 3, and 5-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,818,626. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claims 1-12 of '626 embrace claim 13 is drawn to:

A process for delivering a polynucleotide to a cell comprising: a) forming a complex consisting of a polynucleotide, and a first molecule wherein one or more chelators are covalently linked to the first molecule b) adding to the complex of a) a solution containing one or more metal ions and a second molecule, to which one or more chelators are covalently linked, wherein coordination of one or more metal ions by one or more of the chelators stabilizes the interaction between the first molecule and the second molecule, wherein the first molecule consists of a polycation and the second molecule consists of a polyanion; and, c) delivering the complex of step b) to the cell.

The polycation may be polylysine or polyethylenimine, and the polyanion may be e.g. polyglutamate or a nucleic acid. See e.g. column 12, lines 6-12. the polymers may be copolymers. See column 4, lines 14-18. Claim 8 is included in this rejection because the '626 specification defines a polymer as consisting of at least 80 monomers. See column 4, lines 14-18.

Claims 1, 3, and 5-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 7, 9, 12, 14-18, 20, and 22-24 of copending Application No. 10/795,679. Although the

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conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 6 of '679 is drawn to a method of delivering a nucleic acid to a cell comprising condensing a first polyanion with a polycation to form a particle, adding a second polyanion to the particle to form a complex, wherein at least one of the polyanions is the nucleic acid, and contacting the cell with the complex. In view of claim 14, the first polyanion can be the nucleic acid. In view of claims 9 and 20, the final complex may be negatively charged. The polycation may be polylysine or polyethylenimine. See page 6, lines 28-34, or page 9, lines 1-6. The polyanions may be any of the polyanions of instant claims 5-7. See the specification at page 7, lines 10-19.

### ***Claim Rejections - 35 USC § 102/103***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(f) he did not himself invent the subject matter sought to be patented.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3, and 5-8 are rejected under 35 U.S.C. 102(f) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 6,881,576.

Claim 1 of '576 is drawn to:

1. A process for enhancing delivery of a polyion to a cell, comprising: forming a polyampholyte having a net charge, in the presence of a polyion; and, delivering the complex into a cell.

The specification, in support of this claim, discloses at column 6, lines 44-56 Example 1 which is directed to a general procedure for the formation of a polyampholyte in the presence of DNA:

General procedure for the formation of the polyampholyte in the presence of DNA. (Crosslinking of polycation and polyanion layers on the DNA/PLL/SPLL particles using 1[3-(dimethylamino)propyl]-3-ethyl carbodiimide (EDC) and sulfo-N-hydroxysuccinimide (SNHS). Plasmid DNA (pCiluc) and PLL (M.w. 46 kDa) were mixed in a charge ratio 1:3 (100 ug and 190 ug respectively in 0.5 ml of 20 mM MES, pH 6.5. Succinylated PLL (SPLL) was activated with EDC/SNHS in 50 ul of unbuffered solution at pH 5.0 for 10 min (690 ug SPLL, 1.4 mg EDC, 700 ug SNHS). Then the DNA/PLL complex and activated SPLL were mixed (DNA:PLL:SPLL charge ratio 1:3:10) and the mixture was incubated overnight at room temperature.

Accordingly claim 1 of '576 embraces a method of forming a complex between a nucleic acid and a polycation wherein the complex has a net charge less negative than the nucleic acid, and subsequently associating with that complex a polyanion in sufficient amount to give the complex a net negative charge. The instant claims do not exclude the step of forming a polyampholyte by crosslinking the polyanion to the polycation, so '576 claim 1 and dependents render it obvious, particularly in view of '576 claim 6 which requires delivery of the complex in vivo. The limitations of instant claim 3 (polycation = polylysine or polyethylenimine) are found in '576 claim 2, as is the limitation of instant claim 6, requiring block copolymers. The limitations of instant claim 5 are found in '576 claim 4. Claim 8 is included in this rejection because the ternary complex of '576

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Example 1 appears to comprise a polyanion of at least 80 monomeric units. The polyanion is disclosed at column 6, line 51 as succinylated PLL, and PLL is defined at column 6, line 49 as having a molecular weight of 46 kDa. Assuming a monomer molecular weight of 128 g/mol per lysine monomer, the PLL used is about 360 monomers in length.

However, the inventors of '576 are Jon Wolff, James Hagstrom, Vladimir Budker, and Vladimir Trubetsky, whereas the instant application names these inventors as well as Paul Slattum, Aaron Loomis, and Sean Monahan. As a result it is not clear who has invented the instantly claimed invention.

Claims 1, 3, and 6-8 are rejected under 35 U.S.C. 102(f) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 6,740,643 in view of Lee et al (WO 97/00965, published 1/9/97).

Claim 1 of '643 is drawn to:

A process for obtaining an expression product by delivering a polynucleotide to a cell, comprising: a) associating a noncovalent amphiphilic polyelectrolyte, a cyclodextrin, and a polynucleotide thereby forming a complex, wherein the noncovalent amphiphilic polyelectrolyte consists of a polymeric amphiphile binding agent and charged amphiphiles; and b) delivering the complex to the cell; and, c) expressing the polynucleotide.

It is clear in view of the specification at the paragraph bridging columns 16 and 17 that claim 1 embraces a method of forming a complex between polylysine and a nucleic acid in the presence of a cyclodextrin, and subsequently recharging the complex by addition of a cyclodextrin-epichlorohydrin copolymer that is rendered polyanionic by addition of 4-t-butylbenzoic acid.

'643 does not explicitly teach that recharged complexes must have a net negative charge.

Lee taught that targeted cationic nucleic acid delivery complexes allow non-specific, non-targeted cellular uptake due to the fact that cells generally have a negative surface charge. Despite the presence of a targeting ligand, the charge attraction between positively charged complexes and negatively charged cells leads to non-specific interactions and uptake. Lee taught that this problem could be avoided by rendering targeted delivery complexes negative in net charge. See page 2, lines 11-16, and page 9, lines 18-25.

In view of the '643 specification at column 23, line 51 to column 4, line 50, the claimed compositions may comprise targeting signals. As a result it would have been obvious to one of ordinary skill in the art at the time of the invention to recharge a targeted polycation/nucleic acid complex by addition of an anionic cyclodextrin-epichlorohydrin copolymer, and to adjust the amount of anionic copolymer added such that the final charge of the recharged complex was negative. One would have been motivated to do so in order to increase the efficiency of targeting as taught by Lee above.

Claim 8 is included in this rejection because the '643 specification defines "polymer" at column 26, lines 57-60 as having more than 80 monomers. The term "copolymer" is used to describe the polyanion disclosed at the paragraph bridging columns 16 and 17, so it is considered to have more than 80 monomers.

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The inventors of '643 are Jon Wolff, James Hagstrom, Vladimir Budker, Paul Slattum, David Rozema, and Sean Monahan, whereas the instant application names these inventors, with the exception of Rozema, as well as Vladimir Trubetskoy and Aaron Loomis,. As a result it is not clear who has invented the instantly claimed invention.

Claims 1, 3, and 5-7 are rejected under 35 U.S.C. 102(f) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 6,740,336.

Claim 1 of '336 is drawn to:

A process for generating multilayer particles for delivering a polynucleotide to cell, comprising: condensing a polymer with an oppositely charged polymer to form a particle; and, sequentially adding oppositely charged polymers at the particle forming at least three layers of polymers wherein at least one of the polymers is the polynucleotide.

The specification discloses that the first recited polymer may be a nucleic acid, the second a polycation, and the third, used to recharge the polycation/nucleic acid complex, may be any of the polyanions in instant claims 5-7. See e.g. column 5, lines 1-14:

A wide a variety of polyanions can be used to recharge the DNA/polycation particles comprising: succinylated PLL, succinylated PEI (branched), polyglutamic acid, polyaspartic acid, polyacrylic acid, polymethacrylic acid, polyethylacrylic acid, polypropylacrylic acid, polybutylacrylic acid, polymaleic acid, dextran sulfate, heparin, hyaluronic acid, polysulfates, polysulfonates, polyvinyl phosphoric acid, polyvinyl phosphonic acid, copolymers of polymaleic acid, polyhydroxybutyric acid, acidic polycarbohydrates, DNA, RNA, negatively charged proteins, pegylated derivatives of above polyanions, pegylated derivatives carrying specific ligands, block and graft copolymers of polyanions, any hydrophilic polymers (PEG, poly(vinylpyrrolidone), poly(acrylamide), etc), and other water-soluble polyanions.

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The specification teaches that the polycation may be polylysine or polyethylenimine.

See column 6, lines 6-12 and paragraph bridging columns 11 and 12. Claim 6 requires that the particle formed must be negatively charged. As a result the methods of instant claims 1, 3, and 5-7 are not patentably distinct from those of claims 1-3 of '336.

The inventors of '336 are Jon Wolff, James Hagstrom, Vladimir Budker, Vladimir Trubetskoy, So Chun Wong, and Jason Klein, whereas the instant application names these inventors, with the exception of Wong and Klein, as well as and Aaron Loomis, Sean Monahan, and Paul Slattum. As a result it is not clear who has invented the instantly claimed invention.

Claims 1, 3, and 5-8 are rejected under 35 U.S.C. 102(f) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 6,818,626.

Claims 1-12 of '626 embrace claim 13 is drawn to:

A process for delivering a polynucleotide to a cell comprising: a) forming a complex consisting of a polynucleotide, and a first molecule wherein one or more chelators are covalently linked to the first molecule b) adding to the complex of a) a solution containing one or more metal ions and a second molecule, to which one or more chelators are covalently linked, wherein coordination of one or more metal ions by one or more of the chelators stabilizes the interaction between the first molecule and the second molecule, wherein the first molecule consists of a polycation and the second molecule consists of a polyanion; and, c) delivering the complex of step b) to the cell.

The polycation may be polylysine or polyethylenimine, and the polyanion may be e.g. polyglutamate or a nucleic acid. See e.g. column 12, lines 6-12. the polymers may be copolymers. See column 4, lines 14-18. Claim 8 is included in this rejection because

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the '626 specification defines a polymer as consisting of at least 80 monomers. See column 4, lines 14-18.

The inventors of '626 are Jon Wolff, James Hagstrom, Vladimir Budker, Vladimir Trubetskoy, Paul Slattum, and Sean Monahan, whereas the instant application names these inventors as well as Aaron Loomis. As a result it is not clear who has invented the instantly claimed invention.

Claims 1, 3, and 5-7 are provisionally rejected under 35 U.S.C. 102(f) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over copending Application No. 10/795,679. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 6 of '679 is drawn to a method of delivering a nucleic acid to a cell comprising condensing a first polyanion with a polycation to form a particle, adding a second polyanion to the particle to form a complex, wherein at least one of the polyanions is the nucleic acid, and contacting the cell with the complex. In view of claim 14, the first polyanion can be the nucleic acid. In view of claims 9 and 20, the final complex may be negatively charged. The polycation may be polylysine or polyethylenimine. See page 6, lines 28-34, or page 9, lines 1-6. The polyanions may be any of the polyanions of instant claims 5-7. See the specification at page 7, lines 10-19.

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The inventors of '679 include the inventors of the instant application: Jon Wolff, James Hagstrom, Vladimir Budker, Vladimir Trubetskoy, Paul Slattum, Aaron Loomis, Sean Monahan, as well as So Chun Wong, and Jason Klein. As a result it is not clear who has invented the instantly claimed invention.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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A handwritten signature in black ink, appearing to be 'RS', followed by a long horizontal line extending to the right.

Richard Schnizer, Ph.D.